UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte COLIN STANLEY FITCHETT

Appeal No. 2004-1935
Application No. 09/308,403

ON BRIEF

Before SCHEINER, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-3, 7-26, and 28-59, all of the claims remaining. Claims 1 and 17 are representative and read as follows:

1. A water soluble hemicellulose-based composition comprising:

non-cellulosic, non-starch hemicellulose material;

an oxidase; and

an oxidase substrate;

wherein the hemicellulosic material comprises at least one polysaccharide and at least one polysaccharide is arabinoxylan ferulate.

17. A process for effecting oxidative gelation of a water soluble hemicellulose-based composition comprising non-cellulosic, non-starch hemicellulose material, wherein the hemicellulosic material comprises at least one polysaccharide and at least one polysaccharide is arabinoxylan ferulate, comprising promoting the generation of hydrogen peroxide in situ by redox enzymes, said generation comprising the steps of:

(a) providing oxygen to the composition and/or

(b) providing water to the composition; and/or

(c) providing oxidase substrate to the composition; and/or

(d) activating one or more of the redox enzymes.

The examiner relies on the following references:

Crawford et al. (Crawford)	5,200,338	Apr. 6, 1993
Greenshields et al. (Greenshields)	5,530,112	Jun. 25, 1996

Claims 1-3, 7-26, and 28-59 stand rejected under 35 U.S.C. § 103 as obvious in view of Greenshields and Crawford.

We affirm.

Background

"Plant tissue, especially cell wall material, contains hemicelluloses. The term 'hemicellulose' is a term of art used to embrace non-cellulosic, non-starch plant polysaccharides." Specification, page 1. Arabinoxylan is one important class of hemicellulose. See id. "Phenolic acid (including ferulic acid) and acetyl substituents occur at intervals along the arabinoxylan chains." Page 2.

"Aqueous extracts of many hemicellulose fractions are known to form gels (or viscous media) when treated with oxidizing agents. The phenomenon is known as 'oxidative gelation' in the art but the term is used [in the specification] in a somewhat

broader sense to include the case where viscous solutions are produced rather than true gels." Page 4.

"WO 93/10158 describes oxidative gelation of hemicellulosic material using an oxidizing system comprising a peroxide (such as hydrogen peroxide) and an oxygenase (such as a peroxidase). However, hydrogen peroxide is inconvenient as a reagent in industrial-scale processes, and is potentially dangerous." Page 5.[1]

The specification discloses a method of oxidative gelation of hemicellulosic materials using a combination of a peroxidase enzyme and an oxidase enzyme. See, e.g., page 12: "[T]he invention contemplates a process for effecting oxidative gelation of a hemicellulosic material comprising the step of promoting the generation of hydrogen peroxide in situ by redox enzymes. The redox enzymes preferably comprise an oxidase (e.g., glucose oxidase) and a peroxidase (e.g., horse radish peroxidase), which are preferably present as supplements in the hemicellulosic material." See also page 9: "The material of the invention may further compris[e] an oxidase substrate (e.g. glucose) supplement. If glucose is used, then this has the ancillary advantage of acting as a dispersant."

The specification discloses that the resulting gels or viscous liquids "find a variety of applications [in] various therapeutic, surgical, prophylactic, diagnostic and cosmetic (e.g. skin care) applications." Page 13.

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[1] WO 93/10158, cited in the specification, is the PCT parent application of the Greenshields patent relied on by the examiner.

Discussion

According to Appellant, the claims stand or fall in two groups. See the Appeal Brief, pages 5-6. We will consider claims 1 and 17 as representative.

Claim 1 is directed to a composition comprising a hemicellulosic material that contains arabinoxylan ferulate, an oxidase, and an oxidase substrate. Claim 17 is directed to a method for effecting oxidative gelation of a hemicellulose-based composition; the method comprises promoting in situ generation of hydrogen peroxide by providing oxygen, water, or an oxidase substrate to the composition or activating a redox enzyme in the composition.

The examiner rejected all of the claims as obvious in view of Greenshields and Crawford. See the Examiner's Answer, page 5:

> Greenshields discloses the peroxidase-catalyzed oxidative gelling of feruloylated arabinoxylans from various plant and cereal sources. . . . See, e.g., Abstract; see also col. 5, lines 17-50. Greenshields differs from the claims in that Greenshields adds the peroxidase's substrate, [hydrogen] peroxide, directly to the gelling composition, as opposed to generating the peroxide in situ by adding glucose oxidase and glucose [(an oxidase substrate)], as recited in appellant's claims.
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> However, Crawford clearly discloses that a combination of glucose and glucose oxidase can be used effectively to generate in situ the peroxide required for peroxidase action on a polysaccharide substrate. See col. 6, lines 32-43. Thus, the artisan of ordinary skill at the time of appellant's invention clearly would have recognized that an effective method of generating the peroxide required for peroxidase action in Greenshields' process would have been the generation of the peroxide in situ by adding glucose and glucose oxidase to the gelling composition, as disclosed in Crawford.

We agree with the examiner that Greenshields and Crawford support a prima facie case of obviousness. In Example 1, Greenshields discloses production of a gel from corn bran. The corn bran was ground, treated with cytase enzyme, and extracted

with alkali; then the insoluble cellulose was removed and the supernatant was neutralized. See column 6, lines 13-32. These treatments are disclosed to produce a "hemicellulosic material . . . rich in arabinoxylans and . . . substituted by phenolic acids." Column 2, lines 34-36 (see also column 1, line 46 to column 2, line 33). Greenshields discloses that the soluble, hemicellulosic composition was then gelled by adding horseradish peroxidase and hydrogen peroxide. Column 6, lines 34-40.

As the examiner noted, Greenshields does not teach in situ generation of the hydrogen peroxide required by horseradish peroxidase. However, Crawford teaches that "a continual source of hydrogen peroxide" can be generated "by including a carbohydrate source such as glucose, galactose, or the like, with an appropriate oxidase enzyme such as glucose oxidase, galactose oxidase, etc." Column 6, lines 32-40. Crawford also teaches that exogenously added hydrogen peroxide and in situ-produced hydrogen peroxide are equivalents in a peroxidase-containing composition. See the sentence bridging columns 10 and 11.

Thus, we agree with the examiner that those of ordinary skill in the art would have found it obvious to modify Greenshields' method and composition by substituting an oxidase (e.g., glucose oxidase) and an oxidase substrate (e.g., glucose) for Greenshields' exogenously added hydrogen peroxide, with the expectation that the oxidase would act on its substrate and produce hydrogen peroxide in situ and thereby allow Greenshields' peroxidase-catalyzed polymerization reaction to proceed. Motivation to combine the references is provided by Crawford's disclosure that the oxidase/substrate combination provides a continuous source of hydrogen peroxide and Crawford's disclosure that addition of oxidase and substrate to a peroxidase-catalyzed

reaction is equivalent to addition of exogenous hydrogen peroxide. The combined teachings of the references would have rendered obvious both the composition of claim 1 and the method of claim 17.

Appellant's main argument is that those skilled in the art would not have been led to combine the references. Appellant argues that "Greenshields teaches polymerization of hemicellulose gels, while Crawford teaches a process for depolymerization of lignocellulose. . . . Polymerization and depolymerization are the antithesis of each other." Appeal Brief, page 7. As evidence that those skilled in the art would have found the invention nonobvious, Appellant relies on the declaration (37 CFR § 1.132) of Roderick Greenshields. In his declaration, Dr. Greenshields summarizes the process disclosed in the present application (¶¶ 5 and 11) and the disclosures of the Greenshields and Crawford patents (¶¶ 6-10). Dr. Greenshields concludes (¶¶ 12-13):

> 12. The outcome of the reaction of US'304 [sic, US '403, the instant application] in light of Greenshields et al. and Crawford et al. was unexpected. I would have expected rather that in situ generation of peroxide would depolymerise hemicellulosic material, as had occurred with structurally similar lignin molecules in Crawford et al. In my opinion, the artisan of ordinary skill would also have expected depolymerisation of hemicellulosic material by in situ generation of peroxide.
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> 13. I would also have expected, reading the materials and method in US'403, that depolymerisation of hemicellulosic material by in situ generation of peroxide would occur because of the high levels of glucose/glucose oxidase used. I believe that the artisan of ordinary skill would likewise be surprised that the levels of oxidase and oxidase substrate did not depolymerise the hemicellulosic material of US'403.

Neither Appellant's arguments nor the Greenshields declaration persuade us that those skilled in the art would not have found it obvious to combine the references cited by the examiner. Appellant's position, in a nutshell, is that Greenshields teaches

peroxidase-catalyzed polymerization using exogenous hydrogen peroxide, while Crawford teaches peroxidase-catalyzed depolymerization using hydrogen peroxide generated in situ. Therefore, Appellant and Dr. Greenshields argue, those skilled in the art would have expected that any peroxidase-catalyzed reaction that relied on in situ-generated hydrogen peroxide would be expected to result in depolymerization, not polymerization.

This position is scientifically untenable. It ignores the obviously crucial difference between Greenshields' reaction and Crawford's: they are catalyzed by different peroxidase enzymes. Greenshields uses horseradish peroxidase to catalyze the polymerization of a hemicellulose-containing mixture (see column 6, lines 34-40), while Crawford uses a lignin peroxidase to catalyze depolymerization of lignin (see the abstract). Even the instant specification recognizes that, while hydrogen peroxide is a necessary component of the peroxidase-catalyzed reaction, it is only a substrate – the reaction is catalyzed by the peroxidase enzyme. See the paragraph bridging pages 7 and 8, which shows that peroxidases catalyze reactions of the general formula:

$$H_2O_2 + H_2A \rightarrow 2H_2O + A$$

where H_2O_2 is the chemical formula of hydrogen peroxide and H_2A is an oxidizable substrate.

Thus, those skilled in the art would have expected that horseradish peroxidase, in the presence of hydrogen peroxide, would catalyze the polymerization of Greenshields' hemicellulose-containing composition, regardless of whether the hydrogen peroxide was exogenously added or generated in situ. In other words, while Crawford might teach away from substituting a lignin peroxidase for the horseradish

peroxidase used by Greenshields, it does not teach away from substituting sources of hydrogen peroxide.

It may be true that Dr. Greenshields would have expected in situ peroxide generation to cause depolymerization of hemicellulose, regardless of what peroxidase enzyme was present along with the hydrogen peroxide. However, we do not agree that that expectation would have been shared by a person of ordinary skill in the art because it does not take into account the facts that (1) the polymerization or depolymerization reaction is catalyzed by the peroxidase enzyme in the reaction mixture, not the hydrogen peroxide, and (2) different peroxidase enzymes catalyze different reactions.

Appellant also argues that the specification discloses evidence of unexpected results. See the Appeal Brief, pages 12-13. This argument, however, relies on the same flawed reasoning as the motivation-to-combine argument; that is, Appellant argues that Crawford would have led the skilled artisan to expect depolymerization instead of the observed polymerization. Since we do not agree, for the reasons discussed above, that those skilled in the art would have expected the source of hydrogen peroxide to change the reaction catalyzed by horseradish peroxidase, we do not agree that those skilled in the art would have found the specification's results unexpected.

Appellant also argues that "neither Greenshields nor Crawford disclose or claim a negative feedback loop to ensure that excess hydrogen peroxide production is controlled, as in the claimed invention" and that the references do not teach all the limitations of claim 36. Appeal Brief, pages 9 and 13, respectively.

These arguments are not persuasive. Claim 36 stands or falls with claim 1, so we find it unnecessary to separately consider whether the references would have suggested all of its limitations. Appellant's "negative feedback loop" argument is unpersuasive because that aspect of the disclosed method is inherent to any method that relies on enzymatic generation of hydrogen peroxide. See, e.g., the specification at page 8.

Other Issues

If these claims come before the examiner again, they should be carefully evaluated for compliance with the second and fourth paragraphs of § 112. For example, claims 21 and 49 appear to be exactly the same. Also, the "redox enzymes" recited in claim 18 appear to lack antecedent basis, as do the "dehydrated gel or viscous medium" recited in claim 15 and the "material, gel, viscous medium, [etc.]" recited in claim 24. Finally, claims 25, 47, and 50 do not appear to limit the claims from which they depend, since intended uses do not further limit the claimed subject matter.

Summary

The references cited by the examiner would have suggested the composition of claim 1 and the method of claim 17 to a person of ordinary skill in the art. The examiner's rejection of claims 1 and 17 is affirmed. Claims 2, 3, 7-16, 18-26, and 28-59 fall with claims 1 and 17.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

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